

microRNAs as Regulators of Epigenetic Mechanisms in Chronic Pulmonary Diseases

Dissertation*

zur

**Erlangung der naturwissenschaftlichen Doktorwürde
(Dr. sc. nat.)**

vorgelegt der

Mathematisch-naturwissenschaftlichen Fakultät

der

Universität Zürich

von

Caroline Leuenberger

von

Ursenbach BE

Promotionskomitee

Prof. Dr. med. vet. Max Gassmann

Prof. Dr. med. Malcolm Kohler

Prof. Dr. med. Jan Krütfeldt

Prof. Dr. med. Ralph Schermuly

PD Dr. med. Lars C. Huber (Leitung der Dissertation)

Zürich, 2016

Table of Contents

Acknowledgements	iii
Summary	v
Zusammenfassung	vii
1 Introduction	1
1.1 Thesis motivation	3
1.2 Specific aims	4
1.3 Outline of the thesis	5
2 Background	9
2.1 Chronic obstructive pulmonary disease	11
2.2 Histone deacetylase	14
2.3 Small non coding RNAs	16
2.4 microRNA identification – a computational approach	18
3 miR-223 controls HDAC2 — a novel axis in COPD	25
3.1 Publication	27
3.2 Introduction	28
3.3 Material and Methods	30
3.4 Results	32
3.5 Discussion	39
3.6 Conclusion	42
3.7 Electronic supplementary material	46
4 miR-223: exosomal transport	53
4.1 miR-223 transport	55
5 Synthesis	59
5.1 Synthesis	61
Index of abbreviations	67
Curriculum Vitae	69